Department of Genitourinary Pathology

F. K. Mostofi, M.D.
Chairperson
Date of Appointment - 1 July 1948

MISSION

The department is responsible for clinicopathological studies of five organs: kidney, bladder, prostate, testes, and penis. In line with the mission of the AFIP, the departmental mission is to strive for excellence in consultation, education, and research for the Department of Defense, the Department of Veterans Affairs and other federal agencies, and civilian pathologists and to maintain and expand international research and educational programs.

ORGANIZATION

The department has two divisions: the Nephropathology Division under Dr. Sabnis, reported separately, and Genitourinary Pathology under Dr. Davis, reported here.

STAFF

Medical

F. Kash Mostofi, M.D., Chairperson
Charles J. Davis, Jr., M.D., Deputy Chairperson
Isabell A. Sesterhenn, M.D., Senior Pathologist
Sumitra B. Bawa-Parekh, COL, MC, USA, Staff Pathologist
(D) Tse H. Lin, COL, MC, USA, Staff Pathologist
Kenneth W. Sapp, LCDR, MC, USN, Staff Pathologist
(A) Robert W. Brinsko, LCDR, MC, USN, Staff Pathologist

Technical (Medical) Support

Frank A. Avallone, Research Biologist
Virginia Achstetter, Histopathology Technician
Denise Young, Histopathology Technologist, ARP

Administrative

Walda M. Reese, Administrative Assistant to Chairperson
Annette D. Allen, Secretary

CONSULTATION

Cases	*Received*
Military	1,374
Federal (VA/PHS)	970
Civilian	2,278
Interdepartmental	283

In 92 cases, we had major disagreements with the contributor; in 780 cases, there were minor diagnostic changes; and in 829 cases, no contributor diagnosis was given. We agreed with the

contributor in 2,035 cases; however, in many of these, the contributor, the attending surgeon, or the patient wanted confirmation of the diagnosis by us.

As in the past year, the number of telephone requests has remained high. More than half of our cases necessitated telephone communication, either because the case was sent by Federal Express, the contributor asked for it, there was disagreement, or we needed additional information for proper diagnoses.

As in the past year, most of the surgical consultations were on prostatic biopsies. Because of screening programs, we are seeing biopsy specimens from totally asymptomatic patients who were found to have a nodule on digital rectal examination, elevated PSA, or abnormal ultrasound. These biopsies, especially in a group of young patients from whom six or more biopsy specimens were taken, have led to problems in interpretation because we see changes not seen before. The problem is compounded by the fact that many patients have been pretreated with a variety of new drugs.

Personal consultation by patients or their relatives has increased. Almost every week we have a patient walk in with his slides for a second opinion, or call or write to us for advice as to what to do. This necessitates telephone calls to the contributing pathologist and to the urologist to coordinate advice to the patient.

Frequently we are asked to return the slide on which we have made an official report. In many of these instances we have only one slide, but the patient has been transferred to another urologist who understandably demands to see the slides before the patient is treated. If the slide has more than one section, we try to lift one section off for permanent repository. If this is not feasible, we photograph the lesion and send the slide. When returning the slide (or the block), we have learned to send it by Federal Express, so that the material gets there on time. This necessitates phoning the requestor for his Federal Express number.

Another problem is the discrepancy between the biopsy specimens we diagnosed as exhibiting carcinoma and the prostatectomy specimen that does not show any carcinoma. In these cases, the contributing pathologist usually has sectioned the prostate and may have 70 to 100 slides, and the slides have to be examined. In all such cases, we have found cancer often in one or two slides.

All these activities associated with consultation add to the consultation time.

In all organs we are still very much interested in environmental factors, in manifestations of AIDS, and in suspected virally induced lesions. The following specific lesions are of special interest:

Penis—The number of consultation cases are so few and the available material so scant that we are inclined to accept any cases that are sent. We are especially interested in tissues from patients with venereal diseases, as the frequency of these seems to be on the rise and the diagnosis is often missed or misdiagnosed as lymphoma.

Testes—Testicular tumors in infants and children, delayed chemotherapy failures, and nongerminal tumors.

Prostate—We are in need of biopsy specimens of prostates treated with current antiandrogens and other chemotherapeutic agents. We would like to provide the same service that is provided to the San Diego Naval Medical Center and to the Walter Reed Army Medical Center to other military medical facilities where total prostatectomies are done.

Bladder—Carcinoma in situ remains an enigma for diagnosis, prognosis, and chemotherapy response. The pathology of interstitial cystitis has remained confusing. We would welcome biopsy specimens from such patients to try and clarify the pathology.

Kidney—Tumors in infants and children, adult Wilms' tumors, and certain inflammatory, vascular, drug-induced, and cystic lesions.

RESEARCH

Departmental

Some of the departmental research projects listed in the 1994 report have been completed, and the findings have either been published or accepted for publication.

A. Our studies of various renal tumors in adults, e.g., Wilms' tumor, certain epithelial tumors, multilocular cystic nephroma, and a group of renal hamartomas (angiomyolipoma, capsuloma, and adenoleiomyofibroma) are continuing. In these studies, we need adequate numbers of cases and long-term follow-up. Studies on malignant multilocular cystic nephroma are continuing.

B. The studies on malignant multilocular cysts and renal pelvic hamartomas are in progress.

C. Interphase cytogenetic studies on prostate cancer are on hold due to lack of technical support.

D. Testicular tumors in infants and children. A report of our initial studies has been published. We are now studying gonadal stromal tumors in this age group.

E. Our studies of carcinoma in situ of bladder are continuing.

Cooperative

Intramural Cooperative Studies

The department has two cooperative studies. The study utilizing confocal microscopy in interphase cytogenetics applied to tissue sections has been finalized, and the findings will be submitted for publication. Flow-cytometric analysis of 120 prostatic carcinomas is awaiting correlation of follow-up data and DNA values.

A collaborative study between the Molecular Pathology Division of Cellular Pathology, Gynecologic and Breast Pathology, and Genitourinary Pathology to study interphase cytogenetics and p53 gene mutations in node-positive and node-negative breast cancers is continuing.

Extramural Cooperative Research Projects

Some of the cooperative studies listed in the 1994 report have been completed, and the findings have been published or are in press.

A. Our studies with the U.S. Naval Medical Center and the University of California in San Diego are still on hold, awaiting the report of the NMR finding and three-dimensional reconstruction of NMR images.

B. Our work with the Urology Service and Pathology Department of WRAMC and the Department of Surgery at USUHS on carcinoma of the prostate is continuing. These studies include three-dimensional reconstruction of whole-mount sections of total prostatectomies; comparison of p16 gene alterations in patients who had radical prostatectomy and progressed vs. those without progression; androgen receptor gene amplification in tissue sections of hormonally unresponsive tumors; and angiogenesis in a cohort of 180 patients with follow-up.

C. A joint project with the Radiology Department of Georgetown University is a continuation of the project with Digital Equipment Corporation, Cambridge, Massachusetts, since the medical division of Digital Equipment Corporation was abolished.

D. We have two joint projects with the Urology Service of the U.S. Naval Medical Center in Bethesda on carcinoma in situ of the bladder. One project consists of cytogenetic analysis of archival grade II and III specimens for numerical aberration of chromosomes 1, 7, 9, 10, 15, 17, X, and Y relative to survival and disease progression. This study is continuing. The second study investigates Y chromosome loss in patients with CIS and papillary tumor and CIS with papillary and/or invasive carcinoma.

E. The project with the Georgetown University Department of Urology on chemotherapy of experimentally induced pelvic tumors in mice has been finalized, and a manuscript has been submitted for publication.

GENITOURINARY PATHOLOGY LABORATORY

The laboratory cut 2,552 paraffin blocks for a total of 16,713 slides for various cooperative projects; 679 slides were refurbished or transferred.

For the research on the prostate carcinoma project with Walter Reed Army Medical Center, 924 blocks were prepared from 77 whole prostates and for each block two slides were stained--one for AFIP and one for the WRAMC Pathology Department. Embedding and cutting of total prostate whole-mount sections require a great deal of time and skill. Two thousand five hundred twenty cryostat sections were prepared from 427 prostate biopsy sites for DNA and RNA studies for subsequent use by USUHS.

IMMUNOPATHOLOGY

The laboratory received 203 kidney biopsy specimens on which 2,942 slides were prepared for fluorescent microscopy and immunofluorescence controls.

The laboratory prepared 11,550 immunostains. Interphase cytogenetics by in situ hybridochemistry were prepared on 5,574 slides stained for various chromosomes.

INTERNATIONAL ACTIVITIES

Dr. Mostofi has continued to serve as the head of the World Health Organization (WHO) International Collaborating Center for Genitourinary Tumors, as secretary-treasurer of the International Council of Societies of Pathology (ICSP), and as secretary of the International Society of Urologic Pathology (ISUP).

OTHER ACTIVITIES

Dr. Mostofi has continued to serve as a member of the board of the American Foundation for Urologic Diseases. He has continued to serve on the editorial boards of four journals and as editorial consultant to several others. He is a member of the executive committee of the American Cancer Society Committee on Prostate Cancer, a member of the congressionally mandated committee for research on diseases of the prostate, and a member of the Uniformed Services Urology Group.

Dr. Mostofi reviewed seven manuscripts; COL Davis reviewed eight manuscripts; and Dr. Sesterhenn reviewed six manuscripts for various journals.

SPECIAL AWARDS

Dr. Mostofi received the John Shaw Billings Lifetime Achievement Award.

EDUCATION

During the week of January 23-27, 1995, we gave our week-long Uropathology Course. Dr. Mostofi gave five lectures; Dr. Davis, six lectures; Dr. Sesterhenn, four lectures; Dr. Sapp, one lecture; Dr. Parekh, two lectures; and Dr. Lin, two lectures.

On November 4 and 5, 1995, we gave the weekend Interpretation of Prostatic Biopsy Course, where Dr. Mostofi, Dr. Davis, and Dr. Sesterhenn each gave two lectures.

Urology residents from WRAMC, Brook Army Medical Center, San Diego Naval Medical Center, National Naval Medical Center, and Washington Hospital Center presently spend 1 to 2 months in the department.

GOALS

At the present, we are providing high-quality consultation services. We have no unreported cases more than 30 days old in the department, and our turnaround time in cases that are sent by Federal

Express or Express Mail is 1 day. Our general turnaround time is 8 days. We would like to improve on this.

At the present, we have a very close working relationship with the Urology Services of the Walter Reed Army Medical Center and the San Diego Naval Medical Center. We would like to develop similar relationships with urology services of all military hospitals.

PRESENTATIONS

At the International Conference on Bladder and Prostatic Cancer in Hurghada, Egypt, January 19-21, 1995, Dr. Mostofi gave three lectures: "Pathology of Prostate Cancer and Difficulties in Differential Diagnosis," "Diagnosis of Prostatic Cancer by Guided Needle Biopsy," and "Grading Systems for Classification of Prostatic Carcinoma." Dr. Davis gave two lectures: "Pathology of Bladder Cancer" and "Pathology in Intraepithelial Neoplasia of Bladder." They both participated in two conferences.

On April 12, 1995, at the Fifth Annual Update and Review of Anatomic Pathology Course, Dr. Mostofi, Dr. Davis, and Dr. Sesterhenn each gave one lecture.

In April, Dr. Mostofi and Dr. Sesterhenn attended the 90th Annual Meeting of the American Urological Association in Las Vegas. At the companion meeting of the International Society of Urological Pathology, Dr. Sesterhenn and Dr. Mostofi each discussed the pathology of the two cases presented clinically. At the meeting of the Society for Urology and Engineering, Dr. Sesterhenn gave a lecture on three-dimensional reconstruction of total prostatectomy specimens. Dr. Mostofi presented a poster on "Renal Medullary Carcinoma: The Seventh Sickle Cell Nephropathy," and Dr. Sesterhenn presented a poster on "Metanephric Adenoma: Clinicopathological Study of Fifty Patients." A report on the pathological and clinical findings of TIc prostatic carcinoma was presented. Also, a preliminary report on determination of Y chromosome loss and its prognostic significance in CIS of bladder was presented.

Also in April, Dr. Sesterhenn spoke to the Western New York Society of Pathologists in Buffalo, N.Y., on "Pathology of Tumors of the Testis, Bladder, and Prostate."

In June, Mr. Avallone gave two lectures on "Revisitation of Renal Biopsy Technology." One lecture was to the National Society of Histotechnology, Region II Seminar, in Annapolis, Maryland, and the other was at the Histopathology Seminar at the AFIP.

In July, Dr. Sesterhenn lectured on "Pathology of Bladder Carcinoma" at the Controversies and Recent Advances in Surgical Pathology Course in Snowmass Village, Colorado.

In August, Dr. Mostofi spoke at George Washington University on "Prostatic Intraepithelial Neoplasia."

In October, Dr. Sesterhenn again spoke to the Western New York Society of Pathologists in Buffalo, N.Y., on "Testicular Tumors."

In December, Dr. Mostofi and Dr. Sesterhenn attended the III Congress of Urological Oncology Updates in Caracas, Venezuela. Dr. Mostofi lectured on "New Aspects on Prostate Cancer Pathology," "Histopathologic Assessment of Testis Cancer and Postchemotherapy Metastatic Tumors," and "New Aspects in Bladder Cancer Pathology." Dr. Sesterhenn lectured on "Histopathological Assessment of Radical Prostatectomy Specimens."

Members of our staff also attended various conferences. In January, Dr. Mostofi, Dr. Davis, and Dr. Sesterhenn attended the 1995 Interstitial Cystitis Symposium in Bethesda, Md.

In March, Dr. Mostofi and Dr. Sesterhenn attended the 84th Annual Meeting of the United States and Canadian Academy of Pathology in Toronto, Canada.

In April, Dr. Mostofi attended the board meeting of the American Foundation for Urologic Diseases.

In June, Dr. Mostofi attended the ACS-NPCDP Executive Committee Meeting in Seattle, Washington. And in July, he attended a meeting sponsored by the ACS Advisory Group on Prostate Cancer in Atlanta, Georgia.

In November, Dr. Mostofi attended an International Consultation on Prostatic Intraepithelial Neoplasia and Pathologic Staging of Prostate Cancer and participated in a workshop on defining and addressing the relevance of pathologic staging of prostate cancer at the Mayo Clinic in Rochester, Minnesota.

PUBLICATIONS

Journal Articles

1. Davis CJ Jr, Mostofi FK, Sesterhenn IA. Renal medullary carcinoma: the seventh sickle cell nephropathy. *Am J Surg Pathol.* 1995;19:1-11.
2. Mostofi FK, Murphy GP, Mettlin C, Sesterhenn IA, Batsakis JG, Khaliq SU, Nadimpalli V, Tahan S, Siders DB, Kollin J, Marsh W, Owings M, Sweet J. Pathology review in an early prostate cancer detection prog*ram: results from the American Cancer Society National Prostate Cancer Detection Project. Prostate*. 1995;27:7-12.
3. Davis CJ Jr, Barton JH, Sesterhenn IA, Mostofi FK. Metanephric adenoma: clinicopathological study of fifty patients. *Am J Surg Pathol.* 1995;19:1101-1114.
4. Bauer JJ, Sesterhenn IA, Mostofi FK, McLeod DG, Srivastava S, Moul JW. p53 nuclear protein expression is an independent prognostic marker in clinically localized prostate cancer patients undergoing radical prostatectomy. *Clin Cancer Res.* 1995;1:1295-1300.
5. Epstein JI, Grignon DJ, Humphrey PA, McNeal JE, Sesterhenn IA, Troncoso P, Wheeler TM. Interobserver reproducibility in the diagnosis of prostatic intraepithelial neoplasia. *Am J Surg Pathol.* 1995;19:873-886.
6. Schenkman NS, Sesterhenn IA, Washington L, Tong YA, Weghorst CM, Buzard GS, Srivastava S, Moul JW. Increased p53 protein does not correlate to p53 gene mutations in microdissected human testicular germ cell tumors. *J Urol.* 1995;154:617-621.

In addition, one paper is in preparation and one book chapter is in press.

Abstracts

1. Davis Jr CJ, Sesterhenn IA, Mostofi FK, Barton JH. Metanephric adenoma: clinicopathological study of fifty patients. *J Urol.* 1995;153:N/3. Abstract 117.
2. Davis Jr CJ, Sesterhenn IA, Mostofi FK. Renal medullary carcinoma: the seventh sickle cell nephropathy. *J Urol.* 1995;153:O/3. Abstract 118.
3. Douglas TH, Sesterhenn IA, Moul JW, McLeod DG. The significance of PSA-detected, nonpalpable adenocarcinoma of the prostate (stage T1C). *J Urol.* 1995;153:D/2. Abstract 92.
4. Sesterhenn IA, Mostofi FK, Davis Jr CJ. Determination of Y chromosome loss and its prognostic significance in CIS of bladder. *J Urol*. 1995;153:K/1. Abstract 717.

DIVISION OF NEPHROPATHOLOGY

Sharda G. Sabnis, M.D.
Chief
Date of Appointment - 1 January 1994

MISSION

To excel in the field of nephropathology by providing expertise in consultation, education, and research for the military, federal, and civilian sectors at the national and international level.

STAFF

Medical

Sharda G. Sabnis, M.D., Chief
Tatiana T. Antonovych, M.D., Visiting Scientist

Administrative

Betty B Leinson, Secretary

Dr. Sabnis is registrar, Registry of Nephropathology, of the American Registry of Pathology (ARP). Dr. Sabnis serves as a consultant to the Department of Pathology, National Naval Medical Center (NNMC). She continues as adjunct assistant clinical professor of pathology, Department of Pathology, Georgetown University, and as clinical assistant professor of pathology, Uniformed Services University of the Health Sciences (USUHS). She is a founding member of the International Society of Geriatric Nephrology and Urology and serves as a panelist for the NSAID Renal Pathology Registry Project.

CONSULTATION

Cases Processed

Description	*Received*	*Reported*
Total	490	473
Surgical	442	425
Autopsies	48	48
Military/Federal	159	159
Civilian	331	314
Intramural	57	57
Extramural	90	90

The staff reviewed a total of 637 cases, including 442 surgical cases, 48 autopsies, and 147 intramural and extramural consultations during the year. Among the 490 cases assigned to the division, 355 were received for electron microscopy; however, 390 specimens were studied by electron microscopy, including those that needed additional evaluation. One hundred fifty-one cases were studied by immunofluorescence microscopy, and 48 cases were autopsies. In addition, a

total of 147 intramural or extramural (walk-in) consultations were rendered. In spite of the substantial increase in the number of cases received by the division (343 in 1994, 490 in 1995) and the increase in number of cases studied by electron microscopy, the total case turnaround time was maintained at an average of 8.5 days.

In general, the cases received by the division pose diagnostic problems for the contributing pathologist. It is required that most cases be studied by electron microscopy to reach a conclusive diagnosis, as different renal diseases present with similar clinical symptoms and may have similar morphologic changes by light microscopy. The cases are routinely studied by light and electron microscopy. When tissue is available, immunofluorescence microscopy is performed and immunoperoxidase technique is used where necessary. These cases over the years have been included in various research projects and clinicopathologic studies and have been used as teaching material.

RESEARCH

Major areas of interest were: (1) the effect of partial nephrectomy on the remaining renal parenchyma in baboons, with the Division of Nephrology, University of Miami;(2) the effect of ionizing radiation on various organ systems following the accident at the Chernobyl Nuclear Power Plant (AFIP/Ukraine); and (3) the development of a rat model of IgA nephropathy for the experimental studies evaluating the effects of fish oil, with the Department of Pediatrics, Medical College of Virginia, Richmond, Va. In addition, two intramural projects were initiated and include: focal proliferative glomerulonephritis in the elderly and evaluation of kidney biopsy material to measure levels of lead (Pb) in the renal tissue and correlate with the morphologic changes.

EDUCATION

The division supported the educational objectives of the Institute as follows:

1. Daily microscopic pathology conferences were held for 2 to 3 hours, which provided on-the-job training for nine fellows, both civilian and military personnel, including national and international pathologists and nephrologists.
2. The division continues a monthly teaching session for the fellows, Division of Nephrology, WRAMC.
3. Dr. Sabnis presented cases at the renal biopsy conferences at Walter Reed Army Medical Center, Georgetown University Hospital, and National Naval Medical Center and at the Federal Medical Monthly Nephrology Seminar held by USUHS, Bethesda, Md.
4. Dr. Sabnis presented a series of lectures for the pathology and nephrology residents and fellows on “Medical Renal Diseases,” Department of Pathology, WRAMC, and the Department of Nephrology, Georgetown University.
5. Dr. Sabnis participated in the following AFIP-sponsored activities: prepared materials for the Case for Diagnosis Program, the VA Quality Control Program, AFIP Staff Conference, a lecture series arranged by the American Registry of Pathology for pathology residents, and courses held by the Department of Environmental and Toxicologic Pathology and a course entitled “Problems in Anatomic Pathology.”

GOALS

1. Recruit staff members and fellows into the Division of Nephropathology.
2. Provide best consultation and maintain the improved case turnaround time.
3. Participate in the AFIP educational efforts, provide training to pathologists and nephrologists through lectures and conferences, and continue the Nephropathology course given by the division.

4. Publish results of the research protocols.
5. Continue collaboration on animal research with various universities and develop new collaborative projects within AFIP and other institutions.
6. Present papers at various national and international meetings.

PRESENTATIONS

The following lectures were given by S. G. Sabnis, M.D.:

1. "Medical Renal Diseases," pathology lecture series, Department of Pathology, Walter Reed Army Medical Center, Washington, D.C., January 19, 23, and 26, 1995.
2. "Pathology of Renal Transplants," Division of Nephrology, Francis Scott Key Hospital, Johns Hopkins University, Baltimore, Maryland, February 28, 1995.
3. "Lupus Nephritis," panelist, spring meeting, National Kidney Foundation, Washington, D.C., March 24, 1995.
4. "Drug-induced Nephropathy," AFIP Staff Conference, April 26, 1995.
5. "Nephropathology," Problems in Anatomic Pathology course, AFIP, Washington, D.C., May 5, 1995.
6. "Lead Nephropathy," Analytical and Molecular Biological Techniques in Environmental Toxicology and Pathology course, Department of Environmental and Toxicologic Pathology, AFIP, August 19, 1995.
7. "Pathology of Renal Diseases," Division of Nephrology, Georgetown University, Washington, D.C., August 10 and 17, 1995.
8. "Nephropathology Cases" ARP lectures for pathology residents, AFIP, Washington, D.C., September 15, 1995.

PUBLICATIONS

1. Sabnis SG. Pathology of renal diseases in the elderly. *Geriatr Nephrol Urol.* 1995;5:41-50.
2. Antonovych TT, Sabnis SG. Renal manifestations of systemic lupus erythematosus. In: Antonovych TT, ed. *Pathology of Systemic Lupus Erythematosus.* Washington, DC: Armed Forces Institute of Pathology, American Regisry of Pathology; 1995:11-44.
3. Antonovych TT, ed. *Pathology of Systemic Lupus Erythematosus.* Washington, DC: Armed Forces Institute of Pathology, American Registry of Pathology; 1995.
4. Afrouzian M, Abraham A, Sabnis S. IgD/kappa monoclonal gamopathy and glomerulonephritis. In: Proceedings of the XIII International Congress of Nephrology; July 2-6, 1995; Madrid, Spain.
5. Musio F, Carome MA, Bohen EM, Sabnis S, Yuan CM. The effects of glycine on cisplatin nephrotoxicity and heat shock protein 70 expression in the rat kidney. *J Am Soc Nephrol.* 1995;6:2,985.

In addition, a book chapter is in press.